

It is Claimed:

1. A N-radiohaloaryl-alkylcarboxamide radioligand wherein the alkyl moiety thereof is provided by a branched hydrophobic carbon unit, the hydrocarbon unit formed by acyclic alkyl groups and/or cycloalkanes, the radioligand having a high  
5 affinity to TRP-M8 receptors in cells and tissues and having a specific activity of at least about 20 Ci/mmol or greater, wherein the TRP-M8 affinity is characterized by a K<sub>d</sub> of about  $1 \times 10^{-5}$  or less.
2. The radioligand as in claim 1 wherein the radiohalo moiety is covalently bound in the molecule.
- 10 3. The radioligand as in claim 2 wherein the radiohalo moiety is selected from fluoride and iodide radionuclides.
4. The radioligand as in claim 3 wherein the specific activity is about 20 Ci/mmol or greater.
5. The radioligand as in claim 1 wherein the alkyl moiety is represented by R-, and  
15 wherein R is a saturated or monoethylenically unsaturated alkyl-substituted cyclic or bicyclic alkyl radical containing a total of 7-14 carbon atoms and is selected from the group cyclopentanes, cyclohexanes, cycloheptanes, cyclooctanes, cyclononanes, [3.1.1]bicyclo-heptanes and -hept-5-enes, [2.2.1]bicyclo-heptanes and -hept-5-enes, and [2.2.2]bicyclo-octanes and -oct-  
20 5-enes, the alkyl radical containing from 1 to 3 C<sub>1</sub> – C<sub>5</sub> normal or branched alkyl substituents.

6. The radioligand as in claim 1 wherein the alkyl moiety is a branched chain represented by  $R'R''R'''C-$ , where  $R'$  and  $R''$  are C3 to C5 alkyl (which may be the same or different), and  $R'''$  is hydrogen or a C1 to C5 alkyl, and wherein  $R'$ ,  $R''$  and  $R'''$  provide a total of at least 5 carbons.
7. The radioligand as in claim 1 wherein the aryl moiety is a substituted aromatic radical represented by  $Y-$ , the substituents being represented by  $R_1$ ,  $R_2$ , and  $X$ , wherein
- $R_1$  is selected from the group hydrogen, hydroxyl,  $C_1 - C_5$  alkyl,  $C_1 - C_3$  alkoxy,  $C_1 - C_3$  carboxyalkyl,  $C_1 - C_3$  oxycarbonylalkyl,
- $R_2$  is selected from the group hydrogen, hydroxyl,  $C_1 - C_5$  alkyl,  $C_1 - C_3$  alkoxy, trifluoromethyl, nitro, cyano, halo, and
- $X$  is selected from the group  $[^{18}F]-$ ,  $[^{123}I]-$ ,  $[^{125}I]-$ , and  $[^{131}I]-$ .
8. The radioligand as in claim 7 wherein the aromatic radical includes monoaromatic rings, polyaromatic rings or heterocyclic aromatic rings.
9. Use of the radioligand of claim 1 in radioreceptor assays.
10. Use of the radioligand of claim 1 for scanning or imaging tissues bearing the TRP-M8 receptor.
11. A composition comprising a N-radiohaloaryl-alkylcarboxamide of Formula 1:

Formula 1

**R-CONH-Y**

where (a) **R** is a saturated or monoethylenically unsaturated alkyl-substituted cyclic or bicyclic alkyl radical containing a total of 7-14 carbon atoms selected from the group cyclopentanes, cyclohexanes, cycloheptanes, cyclooctanes, cyclononanes, [3.1.1]bicyclo-heptanes and -hept-5-enes, [2.2.1]bicyclo-heptanes and -hept-5-enes, and [2.2.2]bicyclo-octanes and -oct-5-enes, the alkyl radical containing from 1 to 3 C<sub>1</sub> – C<sub>5</sub> normal or branched alkyl substituents, and (b) **Y** is a substituted aromatic radical containing substituents **R**<sub>1</sub>, **R**<sub>2</sub>, and **X**, wherein

**R**<sub>1</sub> is selected from the group hydrogen, hydroxyl, C<sub>1</sub> – C<sub>5</sub> alkyl, C<sub>1</sub> – C<sub>3</sub> alkoxy, C<sub>1</sub> – C<sub>3</sub> carboxyalkyl, C<sub>1</sub> – C<sub>3</sub> oxycarbonylalkyl,

**R**<sub>2</sub> is selected from the group hydrogen, hydroxyl, C<sub>1</sub> – C<sub>5</sub> alkyl, C<sub>1</sub> – C<sub>3</sub> alkoxy, trifluoromethyl, nitro, cyano, halo, and

**X** is selected from the group [<sup>18</sup>F]-, [<sup>123</sup>I]-, [<sup>125</sup>I]-, and [<sup>131</sup>I]-.

12. The composition as in claim 11 wherein the alkyl radical of (a) contains 8-12 carbon atoms and the total number of carbon atoms in the alkyl substituents on the α- and β-ring carbons are from 1 to 5.

13. The composition as in claim 12 wherein the carboxamide group is in an equatorial position relative to the plane of the cycloalkyl ring.

14. The composition as in claim 11 wherein the Formula 1 compound has a specific activity of about 20 Ci/mmol or greater.

15. The composition as in claim 11 wherein the Formula 1 compound is a ligand for the TRP-M8 receptor.

16. The composition as in claim 15 wherein the Formula 1 compound has a high affinity for the TRP-M8 receptor.

5 17. A composition comprising a branched chain N-radiohalo-substituted-aryl alkylcarboxamide of Formula 2:

#### Formula 2

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where (a)

R' and R'' are C<sub>3</sub> to C<sub>5</sub> alkyl (which may be the same or different), and R''' is hydrogen or a C<sub>1</sub> to C<sub>5</sub> alkyl, and R', R'' and R''' provide a total of at

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least 5 carbons; and (b) Y is a substituted aromatic radical with substituents

R<sub>1</sub>, R<sub>2</sub>, and X, wherein

R<sub>1</sub> is selected from the group hydrogen, hydroxyl, C<sub>1</sub> – C<sub>5</sub> alkyl, C<sub>1</sub> – C<sub>3</sub> alkoxy, C<sub>1</sub> – C<sub>3</sub> carboxyalkyl, C<sub>1</sub> – C<sub>3</sub> oxycarbonylalkyl,

R<sub>2</sub> is selected from the group hydrogen, hydroxyl, C<sub>1</sub> – C<sub>5</sub> alkyl, C<sub>1</sub> – C<sub>3</sub> alkoxy, trifluoromethyl, nitro, cyano, halo, and

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X is selected from the group [<sup>18</sup>F]-, [<sup>123</sup>I]-, [<sup>125</sup>I]-, and [<sup>131</sup>I].

18. The composition as in claim 17 wherein R', R'' and R''' provide a total of 5 to 10 carbons.

19. The composition as in claim 17 wherein

one or both of R' and R'' are branched alkyl radicals selected from the group 2-propyl (isopropyl), 2-butyl (sec-butyl), 2-methyl-1-propyl (iso-butyl), 2-methyl-2-propyl (tert-butyl), 2-pentyl, 3-pentyl, 3-methyl-1-butyl (iso-pentyl), 2-methyl-1-butyl, 3-methyl-2-butyl, 2,2-dimethyl-1-propyl (i.e. neo-pentyl), 1,1-dimethyl-2-propyl

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20. The composition as in claim 17 wherein the Formula 2 compound has a specific activity of about 20 Ci/mmol or greater.

21. The composition as in claim 17 wherein the Formula 2 compound is a ligand for the TRP-M8 receptor.

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22. The composition as in claim 21 wherein the Formula 2 compound has a high affinity for the TRP-M8 receptor.

23. A method for using a radioactive ligand, comprising:

15 providing a N-radiohaloaryl-alkylcarboxamide radioligand wherein the alkyl moiety thereof includes acyclic alkyl groups and/or cycloalkanes, the radioligand having a determinably high affinity to the TRP-M8 receptor in cells and tissues and having a specific activity of at least about 20 Ci/mmol or greater; and,

20 contacting the radioligand with cells or tissues under conditions sufficient to permit specific binding between the radioligand and TRP-M8 receptors if said receptors are carried by the cells or tissues.

24. The method as in claim 23 wherein the high affinity to the TRP-M8 receptors is characterized by a  $K_d$  of about  $1 \times 10^{-5}$  or less.

25. The method as in claim 23 further comprising:

25 determining the amount or presence of TRP-M8 receptors in the cells or tissues of the contacting.